REMARKS

Applicant respectfully requests the Examiner to enter the above amendments and to reconsider the objection and rejection in view of the following remarks and amendments. It is noted that the amendment filed on October 25, 2004 was deemed nonresponsive because the amendments to the claims were believed by the Examiner to broaden the scope of the subject matter presented at the time of the first office action. In response, Applicants have presented new claims 14 to 22 which are directed to methods of treating or inhibiting hyperactive gastrointestinal motility.

Status of Claims

Claims 14 to 22 will be pending after entry of the present amendment. Claims 1 to 13 are being canceled without prejudice and Claims 14 to 22 are being added. Claims 1 to 6 have been rejected under 35 U.S.C. §112, first paragraph.

Amendment

The specification is being amended to clarify in the title and throughout the specification that hyperactive "gastric" motility is hyperactive "gastrointestinal" motility and is therefore not limited to the stomach only. Support for these amendments are found, for example, on page 11, lines 19 to 25 and lines 27 to 29, page 12, lines 20 to 24; page 13, lines 5 to 19; and page 19, lines 5 to 20.

The specification is also being amended to provide a new Abstract Of The Disclosure that relates to the compounds of the formula on page 7 of the specification.

Claims 14 to 22 are new. These claims are supported by the specification, for example at page 11, line 15 to line 25; page 12, line 24; page 6, line 23 to page 9, line 15; and original claims 1 to 6. It is respectfully submitted that the change from hyperactive "gastric" motility to hyperactive "gastrointestinal" motility in Claim 14 does not change the scope of the claims as originally presented as "gastric" was being used to mean "gastrointestinal". See for example, page 12 of the specification, line 24 where "gastrointestinal hypermotility" is used and page 11, line 22 to 25 referring to gastrointestinal conditions.

No new matter is added by the amendments to the specification or claims.

Objection of Disclosure

The disclosure has been objected to because it is "unclear whether Applicant intends to be limited to gastric motility, i.e., motility only associated with the stomach, or gastrointestinal motility." Applicant has amended the title, specification and claims to clarify that the invention is not limited to motility only associated with the stomach. In this regard, hyperactive "gastric" motility has been changed to hyperactive "gastrointestinal" motility.

In view of the amendments being made to the title, specification, and claims, Applicant respectfully requests that this objection be withdrawn.

Rejection Under Section 112

Claims 1 to 6 have been rejected under Section 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The office action makes reference to the factors in In re Wands, 8 USPQ2d 1400 and concludes that "[t]he instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice the instant invention without resorting to undue experimentation." Applicant respectfully traverses this rejection as the specification contains extensive teachings to enable any person skilled in the art to make and use the claimed invention without undue experimentation.

Enablement under Section 112, first paragraph requires that the specification teach those skilled in the art how to make and use the invention without undue experimentation. *Atlas Powder Co. v. E.I. duPont de Nemours & Co.*, 750 F.2d 1569, 1576 (Fed. Cir. 1984). Applicant has fully complied with this legal standard. For example, Applicant fully describes the compounds useful for carrying out the claimed invention (*see e.g.*, page 6, line 23 to page 11, line 5). Additionally, this description of compounds includes examples of specific compounds that fall under the genus described on page 7 for one skilled in the art to use. Moreover, Applicant describes how the compounds useful in the present invention can be synthesized by incorporating by reference U.S. Patent No. 5,565,483 (*see e.g.*, specification, page 6, lines 23 to 26 and '483 patent columns 4 to 12). Applicant also describes various ways in which the compounds can be administered to a mammal in accordance with the claims and provides examples of effective dosing amounts, including for humans (*see e.g.*, page 11, lines 6 to 14,

'483 patent, column 17, lines 1 to 12). Applicant also, via reference to US 5,565,483, discloses useful formulations, that can be administered in the methods of the present invention ('483 patent, col. 16, lines 11 to 51).

In addition to the extensive teachings in the specification, it is noted that one skilled in the art would know how to confirm that the compounds of the present invention are effective in treating hyperactive gastrointestinal motility as recited in the claims without undue experimentation. For example, Applicant discloses on page 19 in the specification, an *in vitro* model for evaluating a compounds ability to inhibit guinea pig ileum tissue contractions induced by KCl or carbachol. This type of model is recognized by those skilled in the art as being useful for evaluating a compounds ability to treat/inhibit gastrointestinal hypermotility as recited in the claims. For example, Applicant submits herewith an article and abstract (Hennig et al. "Quantitative Analysis Of Peristalsis In The Guinea-Pig Small Intestine Using Spatio Temporal Maps", Journal of Physiology (1999) 517.2, pp 575-590, and Toja E., et al. "New classes of antimuscarinic agents endowed with selective antispasmodic properties", Apr (1994) 44(4) pp. 501-509) showing the use of *in vitro* guinea pig ileum models to evaluate compounds for effectiveness in treating gastrointestinal hypermotility. In the abstract by Toja E. et al., it is noted that *in vivo* models are also available for evaluating effectiveness for treating hypermotility. Thus, it is respectfully submitted that Claims 14 to 22 fully comply with the enablement requirement of Section 112, first paragraph as one skilled in the art would be able to make and use the full scope of the claimed invention without undue experimentation.

Additionally, it is emphasize that nothing in Section 112, first paragraph, requires an Applicant to provide data in the specification to convince a person skilled in the art that the assertions in the specification are correct. In fact, case law holds that a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must be taken as in compliance with the enabling requirement of the first paragraph of Section 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.*" *See e.g., Fiers v. Revel,* 25 USPQ2d 1601, 1607 (Fed. Cir. 1993). Here, there is no reason to doubt nor has the office action provided reasons to doubt the statements contained in the specification concerning the effectiveness of the methods of the present invention for treating hyperactive gastrointestinal motility. In fact, Applicants provide data on page 19 of the specification that shows KCNQ channel opener

retigabine inhibits guinea pig ileum tissue contractions. Thus, the claims, as amended, fully comply with Section 112, first paragraph.

In view of the foregoing remarks, Applicant respectfully submits that Claims 14 to 22 fully comply with the requirements of Section 112, first paragraph. Accordingly, Applicant respectfully requests that the rejection under Section 112, first paragraph be withdrawn.

CONCLUSION

Applicant respectfully requests entry of the present amendment and withdrawal of all outstanding objections and rejections. Early and favorable notification of allowance of all pending claims is earnestly requested.

Respectfully Submitted,

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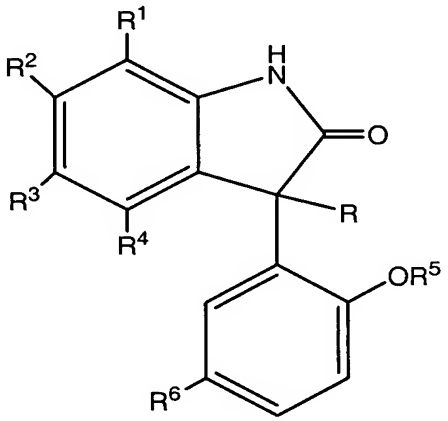
(NEW)

ABSTRACT OF THE DISCLOSURE

This invention provides methods for treating, inhibiting, preventing and ameliorating hyperactive gastrointestinal motility in a mammal utilizing compounds having the formula:



where R, and R^1 to R^6 are described herein. The hyperactive gastrointestinal motility may be associated with, for example, irritable bowel syndrome, Crohn's Disease, colitis, diarrhea, abdominal pain associated with diarrhea, postprandial urgency, or postprandial accentuation of diarrhea or abdominal pain.

EXHIBIT A

Amendments to Specification Relative to Amendment Filed October 25, 2004

On page 1 of the specification, as amended October 25, 2004, please replace the title with the following amended title:

METHODS FOR TREATING ~~GASTROINTESTINAL CONDITIONS~~ HYPERACTIVE GASTROINTESTINAL MOTILITY

Please replace the paragraph beginning on page 1, line 12 and ending on line 17, as amended October 25, 2004, with the following amended paragraph:

This invention relates to novel methods for modulating gastrointestinal tissues utilizing compounds which modulate the KCNQ family of potassium channels, particularly compounds which open or agonize the channels. The methods of this invention include the treatment, prevention, inhibition and amelioration of ~~gastrointestinal conditions such as~~ hyperactive ~~gastric~~ gastrointestinal motility, including that associated with colitis, Irritable Bowel Syndrome and Crohn's Disease.

Please replace the paragraph on page 3, beginning at line 11 and ending at line 22 with the following amended paragraph:

This invention comprises methods for treating, preventing, inhibiting, alleviating or controlling hyperactive ~~gastric~~ gastrointestinal motility in a mammal, the methods comprising administering to a mammal in need thereof a pharmaceutically effective amount of a compound which acts as an agonist or opener of the KCNQ family of potassium channels, including the KCNQ2, KCNQ3, KCNQ4, and KCNQ5 potassium channels, alone or in combination. A particular embodiment of this invention includes use in the methods described herein of one or more agonists or openers of KCNQ2/3 potassium channels. Another series of methods of this invention comprises use of one or more agonists or openers of KCNQ3/5 potassium channels. Further methods of this invention comprise treatment of the bladder instability conditions described herein by pharmaceutical administration of one or more agonists or openers of KCNQ4 potassium channels.

EXHIBIT A

Amendments to Specification Relative to Amendment Filed October 25, 2004

Please replace the paragraph on page 3, beginning at line 24 and ending at line 26 with the following amended paragraph:

Specific methods of this invention include the treatment, prevention, inhibition, alleviation or control of hyperactive ~~gastric~~ gastrointestinal motility associated with colitis, irritable bowel syndrome (IBS) or Crohn's Disease.

Please replace the paragraph on page 11, beginning at line 16 and ending at line 25 with the following amended paragraph:

The methods of this invention are useful for treating, preventing, inhibiting or ameliorating hyperactive ~~gastric~~ gastrointestinal motility in a mammal, the methods each comprising administering to a mammal in need of such treatment a pharmaceutically effective amount of a KCNQ potassium channel opener, as described above. The conditions which may be treated with the methods of this invention include irritable bowel syndrome, also known as spastic colon, Crohn's Disease and mucous colitis. The methods of this invention may also be used for mammalian gastrointestinal (GI) conditions including diarrhea, chronic diarrhea, acute ~~diarhea~~ diarrhea, abdominal pain associated with diarrhea, postprandial urgency, postprandial accentuation of diarrhea or abdominal pain, or a combination of two or more of these symptoms.

Please replace the paragraph beginning at page 14, line 36 and ending at page 15, line 14 with the following amended paragraph:

As used herein, the terms "pharmaceutically effective amount" or "therapeutically effective amount" mean the total amount of each active component of the pharmaceutical composition or method that is sufficient to show a meaningful patient benefit, i.e., treatment, prevention or amelioration of hyperactive ~~gastric~~ gastrointestinal motility or the excessive or undesirable urge to defecate, or a decrease in the frequency of incidence of fecal incontinence. When the malady in question warrants, a pharmaceutically or therapeutically

EXHIBIT A

effective dose may be considered the minimal amount of the compound in question which will alleviate, inhibit or remove the cramping, pressure, pain or feeling of fecal urgency associated with hyperactive ~~gastric~~ gastrointestinal motility. When applied to an individual active ingredient, administered alone, the term refers to that ingredient alone. When applied to a combination, the term refers to combined amounts of the active ingredients that result in the therapeutic effect, whether administered in combination, serially or simultaneously.

Please cancel the Abstract Of The Disclosure in its entirety, and add the attached new Abstract Of The Disclosure.